

Remarks

Claims 1, 3-17, 21, 30-34, 36, and 37 are pending in the subject application. Applicant gratefully acknowledges the Examiner's withdrawal of the rejections under 35 USC §103(a). By this Amendment, Applicant has amended the specification to correct an inadvertent typographical error and to indicate that the subject application is the U.S. national stage application of International patent application No. PCT/GB98/02214 as the first paragraph of the specification. In addition, Applicant has amended claims 1, 5, 7, 10, 11, 32, and 36. Support for the amendments can be found throughout the subject specification and in the claims as originally filed. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 1, 3-17, 21, 30-34, 36, and 37 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

As an initial matter, Applicant's representatives would like to thank Examiner Sisson for the courtesy of the interview conducted on April 27, 2005. Applicant respectfully submits that the amendments to the claims and specification and the remarks presented herein are in accordance with the substance of the interview conducted with the Examiner and that the subject application is in condition for allowance. For example, the claims have been amended to delete reference to "enzyme" where a polymerase is being referenced.

The application is objected to on the grounds that the subject specification fails to comply with the sequence requirements as set forth at 37 CFR 1.821 through 1.825 as set forth on the Notice to Comply attached with the Action. Applicant notes that an Amendment Under 37 CFR §1.825 (a) Through (c) was submitted when the subject application was filed directing entry of page 16 (*i.e.*, Sequence Listing) into the specification. In accordance with the Examiner-Initiated Interview Summary dated April 1, 2005, Applicant is providing with this Amendment a duplicate of the Sequence Listing in computer readable format. Accordingly, reconsideration and withdrawal of the objection is respectfully requested.

Claims 1, 3-8, 30-34, 36, and 37 are rejected under 35 USC §112, first paragraph, on the grounds they contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention and on the grounds that the claims are not enabled by

the subject specification. Specifically, the Examiner indicates that the subject specification does not contain a reproducible method whereby any nucleic acid could be sequenced to completion, wherein the length of the nucleic acid can be unlimited, and wherein the nucleic acid can be “present in a heterogeneous mixture of other polynucleotides, and/or where all possible nucleotides are present and nascent sequences are allowed to develop unimpeded.” The Examiner also asserts, at least in regard to claim 7, that the subject specification speculates as to the ability to practice certain elements of the invention and, therefore, does not teach that the inventors were in possession of the claimed invention as of the filing date of the application. The Examiner also asserts that the specification does not enable the claimed method whereby dual blocking groups are utilized and can be selectively removed.

Applicant respectfully asserts that there is adequate written description in the subject specification to convey to the ordinarily skilled artisan that they had possession of the claimed invention and that the claims are enabled by the subject specification. Applicant notes that claim 1 has been amended to clarify that, in practicing the claimed method, each complementary nucleotide that is incorporated during the processing of the polymerase is detected. This provides that the nucleotide sequence of the polynucleotide can be determined regardless of the speed of the reaction.

In regard to the issue of polynucleotide length, Applicant respectfully asserts that the claimed method can be used with any length polynucleotide. There is no evidence to suggest an upper limit on length of the polynucleotide that can be sequenced using the claimed method. The Examiner also indicates that the issue of length of the polynucleotide also raises the possibility of self-self duplex formation. Applicant respectfully notes that polymerases can “undo” self-self duplexes and continue processing along the polynucleotide strand.

In regard to the issue of sequencing a target polynucleotide in a heterogeneous mixture of polynucleotides, Applicant respectfully points out that the claimed method utilizes surface plasmon resonance (SPR) to measure a change or absorption of radiation that occurs during the interaction of the polymerase, the target polynucleotide, and the complementary nucleotide that is incorporated into the nascent polynucleotide during the sequencing reaction. Applicant respectfully submits that SPR is conducted at a very localized region on the solid support and, therefore, can be used in

measurements at the single molecule level. Support for this can be found in the subject specification at, for example, page 5, lines 21-33, and page 6, lines 7-14.

Also under these rejections, the Examiner asserts that the claims can be interpreted as encompassing binding of the polymerase to a target polynucleotide where the polynucleotide is bound directly or indirectly to the support. By this Amendment, Applicant has amended claim 1 to specify that the polymerase is itself immobilized on the solid support. Applicant notes, however, that the immobilization of the polymerase to the solid support can be either through direct binding to the support, or through indirect binding, such as by a linker molecule attached to the support wherein the polymerase is bound to the linker molecule. The Examiner also questions whether sequencing using the claimed method can occur where all possible nucleotides are present in the reaction mixture but wherein the nucleotides do not contain blocking groups. Applicant respectfully asserts that all nucleotides can be present and unblocked in the claimed method. In this situation, the polymerase reaction will occur at a faster rate and, therefore, detection can be achieved using appropriate readout technology.

In regard to claim 7, the Examiner indicates that the subject specification does not provide support for the method where nucleotides that are blocked at both the 3' and 5' end are utilized since it is not clear that the blocking groups can be selectively removed. Applicant respectfully asserts that the subject specification does teach that blocking groups can be used that can be selectively removed based on their spectral absorbance. See, for example, the middle of page 8 through to the middle of page 9 and page 12 of the subject specification which teach 3' and 5' blocking groups and selective removal thereof.

Applicant respectfully asserts that the claims do find written description and are enabled by the subject specification. In view of the above, reconsideration and withdrawal of the rejections under 35 USC §112, first paragraph, is respectfully requested.

Claims 1, 3-8, 30-34, 36, and 37 are rejected under the judicially created doctrine of "obviousness-type" double patenting over claims 1-5 of U.S. Patent No. 6,623,929. Applicant respectfully traverses and asserts that the claims are not obvious over the cited patent. Applicant respectfully asserts that the claims in the subject application are patentably distinct from the claims of the '929 patent. Claim 1 of the '929 patent is not directed to a method of sequencing; rather,

claim 1 of the '929 patent is directed to a method of polynucleotide synthesis. Moreover, the method of the '929 patent requires modulating the conformation of the polymerase using monochromatic light. Claim 1 of the subject application does not recite an element or limitation wherein the conformation of the polymerase is modulated by monochromatic light. In addition, the claims of the '929 patent do not teach or suggest detecting the interaction between polymerase, the target polynucleotide and the complementary nucleotide. Accordingly, Applicant respectfully asserts that the claims of the subject application are not obvious over the claims of the '929 patent. Reconsideration and withdrawal of the rejection is respectfully requested.

Claims 1, 3-8, 30-34, 36, and 37 are provisionally rejected under the judicially created doctrine of "obviousness-type" double patenting over claims 1, 9, 11, 12, 16, 17, 21, and 22 of co-pending Application No. 10/478,036. Applicant respectfully traverses and asserts that the claims of the subject application are not obvious over the claims of the '036 application. Claim 1 of the subject application relies upon SPR to detect a change in or absorption of radiation that occurs during interaction of the polymerase, the target polynucleotide, and the complementary nucleotide. Claim 1 of the '036 application relies on measurement of a non-linear optical signal or a linear signal coupled to a non-linear signal. Claim 21 of the '036 application further recites that the claimed method can further comprise the application of localized SPR. In the claimed method of the '036 application, SPR may be used to enhance the signal to be detected (see, for example, page 9, lines 28-32, of the '036 application) but SPR does not replace the signal and is not used in the actual detection. Thus, the claims in the '036 application do not teach or suggest the use of SPR to detect a change in or absorption of radiation that occurs during interaction of the components used in the method. Accordingly, Applicant respectfully asserts that the claimed method of the subject application is not obvious over the claims of the '036 application. Reconsideration and withdrawal of the rejection is respectfully requested.

Claims 1, 3-8, 30-34, 36, and 37 are provisionally rejected under the judicially created doctrine of "obviousness-type" double patenting over claims 1-18 of co-pending Application No. 10/786,951. In order to expedite prosecution of the subject application to completion, Applicant has submitted a Terminal Disclaimer with this Amendment which obviates this rejection. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicant's agreement with or acquiescence in the Examiner's position.

In view of the foregoing remarks and amendments to the claims, Applicant believes that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicant invites the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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Attachments: Terminal Disclaimer; Sequence Listing in computer readable format